DRAFT 10/16/2000

Science Advisory Board (SAB)
Dioxin Reassessment Review Committee
Open Meeting, November 1-2, 2000
Ramada Plaza Hotel Pentagon,
4641 Kenmore Avenue, Alexandria, VA.
SAB Web Site http://www.epa.gov/sab

Review of EPA's Draft Revised Dioxin Assessment

DAY 1

8:45 AM Introduction - Dr. Morton Lippmann (Chair)

8:55 AM Member/Consultant Introductions; Conflict of Interest Statements; and comments on report preparation- Designated Federal Official - Mr. Samuel Rondberg

9:30 AM EPA briefing on major issues – Drs. William Farland, EPA National Center for Environmental Assessment

10:15 AM Break

10:30AM Public Comment (AS OF 10/15)

Dr. Gary Kayajanian
Dr. Robert Musil, Physicians for Social Responsibility
Dr. Clifford Firstenberg, Firstenberg Consulting
Professor Thomas Sutter, Pentachlorophenol Task Force.
Dr. Barbara Petersen, Food Industry Dioxin Working Group
Lesa L. Aylward, M.S., BBL Sciences
Marcie Francis, Chlorine Chemistry Council
John Festa, American Forest & Paper Association
James Branum
Carol Wild Scott, Esq. Veterans Consortium Pro Bono Program
Dr. Russ Keenan, Polychlorinated Biphenyls Panel, American Chemistry Council
Laurie Valeriano, Policy Director, Washington Toxics Coalition
Kim Kelly, Endometriosis Association
Dr. Arnold Schecter, University of Texas School of Public Health at Dallas
Dr. T. Webster, Boston University School of Public Health
Dr. Jack S. Mandel, Group Vice President, Exponent

Steven Lester, Children's Environmental Health Network
Dr. J. Donald Millar, Public Health Policy Advisory Board

12:00 Noon Lunch in meeting room

(NB Lead Discussant noted with *)

12:45 PM **Body Burdens**
(Question 1) Did EPA adequately justify its use of body burden as a dose metric for inter-species scaling? Should the document present conclusions based on daily dose? ***Liu*, Crump, Ringen***

1:10PM **Use of Margin of Exposure Approach**
(Question 2) Has EPA's choice of the MOE approach to risk assessment adequately considered that background levels of the dioxins have dropped dramatically over the past decade, and are continuing to decline? How might the rationale be improved for EPA's decision not to calculate an RfD/RfC, and for the recommended MOE approach for conveying risk information? Is an MOE approach appropriate, as compared to the traditional RfD/RfC? Should the document present an RfD/RfC?" ***Brown*, Kim***

1:40PM **(Question 3)** The SAB commented that previous dose-response modeling was too limited to biochemical endpoints (CYPIA1, IA2, . . .). Are the calculations of a range of ED_{01} body burden for non-cancer effects in rodents responsive and clearly presented? Please comment on the weight of evidence interpretation of the body burden data associated with a 1% response rate for non-cancer effects that is presented in Chapter 8, Appendix I and Figure 8-1 (where EPA considers that the data best support a range estimate for ED_{01} body burdens between 10 ng/kg to 50 ng/kg). ***Crump*, Greenlee, Weiss***

2:10PM **Mechanisms and Mode of Action**
(Question 4) How might the discussion of mode of action of dioxin and related compounds be improved? ***Umbreit*, McConnell, Perdew***

2:35PM **(Question 5)** Despite the lack of congener-specific data, does the discussion in the Integrated Summary and Risk Characterization support EPA's inference that these effects may occur for all dioxin-like compounds, based on the concept of toxicity equivalence? ***Albert*, Umbreit, Perdew***

3:00PM Break

3:15PM **Toxicity Equivalence Factors**
(Question 6) Is the history, rationale, and support for the TEQ concept, including its limitations and caveats, laid out by EPA in a clear and balanced way in Chapter 9? Did EPA clearly describe its rationale for recommending adoption of the 1998 WHO TEFs? ***Weiss*, Perdew, Lambert***

3:40PM **(Question7)** Does EPA establish clear procedures for using, calculating, and interpreting toxicity equivalence factors? ***Paustenbach*, Ringen, McKone***

4:05PM **Non-cancer Effects**
(Question 8) Have the available human data been adequately integrated with animal information in evaluating likely effect levels for the non-cancer endpoints discussed in the reassessment? Has EPA appropriately defined non-cancer adverse effects and the body burdens associated with them? Has EPA appropriately reviewed, characterized, and incorporated the recent epidemiological evidence for non-cancer risk assessment for human populations? ***Weiss*, Matanoski, Clapp, Albert***,

4:35PM **(Question 9)** Do reviewers agree with the characterization of human developmental, reproductive, immunological, and endocrinological hazard? What, if any, additional assumptions and uncertainties should EPA embody in these characterizations to make them more explicit? ***McConnell*, Graham, Brown***

5:05PM Adjourn

DAY 2

8:45AM Opening Comments/Questions

8:50AM **Cancer Effects**
(Question 11) Does the document clearly present the evolving approaches to estimating cancer risk (e.g., margin of exposure and the LED_{01} as a point of departure), as described in the EPA "Proposed Guidelines for Carcinogenic Risk Assessment" (EPA/600/P-92/003C; April 1996)? Is this approach equally as valid for dioxin-like compounds? Has EPA appropriately reviewed, characterized, and incorporated the recent epidemiological evidence for cancer risk assessment for human populations? ***Graham*, Matanoski, Clapp, Greenlee***

9:20PM **(Question12)** Please comment on the presentation of the range of upper bound risks for the general population based on this reassessment. What alternative approaches should be explored to better characterize quantitative aspects of potential cancer risk?

Is the range that is given sufficient, or should more weight be given to specific data sources? ***Crump*, Kim, Liu***

10:00AM Break

10:15AM **(Question 10** Do you agree with the characterization in this document that dioxin and related compounds are carcinogenic hazards for humans? Does the weight-of-the-evidence support EPA's judgement concerning the listing of environmental dioxins as a likely human carcinogen? ***Brown*, Crump, Matanoski, Umbreit***

10:45AM **Background and Population Exposures**
(Question 13) Have the estimates of background exposures been clearly and reasonably characterized? ***Thomas*, McKone***

11:10AM **(Question 14)** Has the relationship between estimating exposures from dietary intake and estimating exposure from body burden been clearly explained and adequately supported? Has EPA adequately considered available models for the low-dose exposure-response relationships (linear, threshold, "J" shaped)? ***McKone*, Thomas, Paustenbach***

11:35AM **(Question 15)** Have important 'special populations' and age-specific exposures been identified and appropriately characterized? ***Kim*, Morandi, McConnell***

12:00 Noon Lunch in meeting room

12:45PM **Children's Risk**
(Question 16) Is the characterization of increased or decreased childhood sensitivity to possible cancer and non-cancer outcomes scientifically supported and reasonable? Is the weight of evidence approach appropriate? ***Lambert*, Matanoski, Luster***

1:15PM **Relative Risks of Breast Feeding**
(Question 17) Has EPA adequately characterized how nursing affects short-term and long-term body burdens of dioxins and related compounds? ***Kim*, Morandi, Lambert***

1:40PM **Risk Characterization Summary Statement**
(Question 18) Does the summary and analysis support the conclusion that enzyme induction, changes in hormone levels, and indicators of altered cellular function seen in humans and laboratory animals, represent effects of unknown clinical significance, but they may be early indicators of toxic response? ***Greenlee*, Graham, Albert***

2:10PM **(Question 19)** Has the short summary statement in the risk and hazard characterization on page 107 adequately captured the important conclusions, and the areas where further evaluation is needed? What additional points should be made in this short statement? ***Ringen*, Luster, Paustenbach, Lambert***

2:45PM Break

3:00PM **Sources**
(Question 20) Are these sources adequately described and are the relationships to exposure adequately explained? ***Thomas*, Liu, Morandi***

3:25PM **General Comments**
(Question 21) Please provide any other comments or suggestions relevant to the two review documents, as interest and time allow. ***Lippmann*, Committee***

4:00PM Final Issues/Report Preparation ***Lippmann*, Committee, DFO***

5:00PM Adjourn